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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/035,216	01/04/2002	E. Antonio Chiocca	0609.5050005/JAG/KRM/FRC	3452
26111	7590	04/03/2006	EXAMINER	
STERNE, KESSLER, GOLDSTEIN & FOX PLLC 1100 NEW YORK AVENUE, N.W. WASHINGTON, DC 20005			SULLIVAN, DANIEL M	
			ART UNIT	PAPER NUMBER
			1636	

DATE MAILED: 04/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/035,216

Applicant(s)

CHIOCCA ET AL.

Examiner

Daniel M. Sullivan

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 January 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 40-45 and 47-57 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 40-45, 47-57 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This Office Action is a reply to the Paper filed 4 January 2006 in response to the Non-Final Office Action mailed 9 August 2005. Claims 40-57 were considered in the 9 August Office Action. Claim 46 was cancelled and claim 40 was amended in the 4 January Paper. Claims 40-45 and 47-57 are pending and under consideration.

Response to Amendment and Arguments

Rejection of claim 46 is rendered moot by the cancellation thereof.

Claim Rejections - 35 USC § 112

Rejection of claims 40-45 and 49-57 under 35 U.S.C. 112, first paragraph, as lacking enablement for the full scope of the claimed subject matter is **withdrawn** in view of the amendment to claim 40.

Rejection of claims 40-45 and 49-57 under 35 U.S.C. 112, second paragraph, as being indefinite is **withdrawn** in view of the amendment to claim 40.

Claim Rejections - 35 USC § 103

Claims 40-45 and 47-56 **stand rejected** under 35 U.S.C. 103(a) as being unpatentable over Kim *et al.* (1998) *Genome Res.* 8:404-412 in view of Wang *et al.* (1996) *J. Virol.* 70:8422-8430 as evidenced by Woodfield *et al.* (2000) *Nucl. Acids Res.* 28:3323-3331 for the reasons set forth in the 9 August Office Action commencing at page 8 and herein below in the response to Applicant arguments.

Claims 40, 56 and 57 **stand rejected** under 35 U.S.C. 103(a) as being unpatentable over Kim *et al.* (*supra*) in view of Wang *et al.* (*supra*) and further in view of Saeki *et al.* (1998) *Hum. Gene Ther.* 9:2787-2794 for the reasons set forth in the 9 August Office Action commencing at page 12 and herein below in the response to Applicant arguments.

Response to Arguments

In response to the *prima facie* rejection of record, Applicant does not deny that the combined teachings of the cited art contain all of the elements of the claimed invention but contends that the skilled artisan would not have been motivated to combine the teachings. To support this position, Applicant first quotes a passage from the Office Action stating the nature of the problem to be solved in the method of Kim *et al.* and contends that no motivation can be found in the nature of the problem to be solved because Kim *et al.* has adequately solved the problem. See bridging pages 9-10. In the subsequent paragraphs, Applicant contends that Kim *et al.* demonstrates that the system set forth in the reference had more than adequately solved the problem of providing BAC clones comprising genomic DNA inserts with the capacity to transform sufficient numbers of mammalian cells for functional analysis of the cloned inserts.

This argument has been fully considered but is not deemed persuasive. It is first noted that the passage cited by Applicant is a fragment of sentence and is quoted out of context. The complete passage is found on page 10 of the 9 August Office Action and reads in full:

Motivation to combine these teachings comes from the nature of the problem solved in the method of Kim *et al.*, which is to provide BAC clones comprising genomic DNA inserts with the capacity to transform sufficient numbers of mammalian cells with for functional analysis of the cloned inserts; the inefficiency of transfection using BAC vectors retrofit with only selectable

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markers as taught by Kim *et al.*, which necessitated time consuming and expensive antibiotic selection of transformed cells; and the very high gene transfer efficiency of the amplicon vector of Wang *et al.*, which would allow the skilled artisan to obtain a large number of mammalian cells comprising BAC clones without the need for antibiotic selection.

Thus, viewed in context, it is clear that the nature of the problem to be solved in the method of Kim *et al.* is only one of the facts, which, viewed as a whole, provide motivation to combine the teachings of the cited art. Applicant's position appears to be that once a method is developed to the point that it is operative one of skill in the art would not be motivated to improve the method. On the contrary, as stated in MPEP §2144, "The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. *In re Sernaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983)." Thus, if the teachings found in the art express or imply some advantage or beneficial result of combining the teachings found therein, the skilled artisan would be motivated to combine the teachings. There is no requirement that a technology disclosed in a reference be wholly inoperative for its intended purpose or that an author or inventor explicitly state dissatisfaction with the functioning of their technology in order for the skilled artisan to be motivated to improve the technology. What is required for motivation is that the skilled artisan perceives some advantage or beneficial result of combining the teachings of the art. When the teachings of Kim *et al.* and Wang *et al.* are viewed as a whole, the skilled artisan would clearly perceive an advantage in using the amplicon vector of Wang *et al.*, which would allow the skilled artisan to obtain a large number of mammalian cells comprising BAC clones without the need for antibiotic selection, as compared with the relatively

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inefficient method of transfection using BAC vectors retrofit with only selectable markers as taught by Kim *et al.*

Next, Applicant contends that one of skill in the art would not have been motivated to improve the efficiency with which the vectors of Kim *et al.* are transfected into cells or reduce the expense associated with antibiotic selection. Applicant's reasoning is that Kim *et al.* does not explicitly state that the method of introducing BAC clones into mammalian cells was inefficient but merely notes that the efficiencies ranged from 1% to 6%. Applicant contends, "Efficiency, in the context of cell transfection, is a relative variable that is dependent upon the particular cells used and the nature of the transfected nucleic acid construct. A transfection efficiency of 1% may in fact be considered very high depending on the particular cells and nucleic acid constructs used."

This argument is not deemed persuasive. Applicant's point that efficiency, in the context of cell transfection, is a relative variable that is dependent upon the particular cells used and the nature of the transfected nucleic acid construct is accurate. However, in the instant case, the relevant comparison is between the antibiotic resistance gene retrofitted BAC clones of Kim *et al.* and the amplicon vector of Wang *et al.* As Applicant acknowledges, Kim *et al.* teaches a transfection efficiency of 1% to 6% in SW480 cells and murine NIH-3T3 cells. As stated in the 9 August Office Action (page 9), "Wang *et al.* teaches a hybrid herpesvirus amplicon vector comprising herpesvirus cleavage/packaging sequence and a herpesvirus origin of replication...which is demonstrated to provide highly efficient delivery of DNA into a wide range of human cells (see especially Table 2)." A review of Table 2 shows that Wang *et al.* tested the amplicon vector described therein in fourteen distinct cell lines and obtained an

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infection efficiency of greater than 80% in all but two of them, which exhibited an efficiency of 50%-60%. Thus, the skilled artisan considering the teachings of Kim *et al.* and Wang *et al.* as a whole would clearly view the transfection efficiency of the antibiotic resistance gene retrofitted BAC vector of Kim *et al.* as inefficient relative to the amplicon vector of Wang *et al.* and would therefore perceive an expected benefit in substituting the amplicon vector.

Next, Applicant again argues that the transfection efficiencies obtained with the antibiotic resistance gene retrofitted BAC clones are more than adequate for purposes of detecting and analyzing the expressed transgenes. However, as discussed above, the relevant question is not whether the vector of Kim *et al.* is “adequate” or “inadequate”, but whether the skilled artisan would perceive any benefit in substituting the amplicon vector of Wang *et al.* Even if one were to accept that the antibiotic resistance gene retrofitted BAC vector of Kim *et al.* was “adequate”, for the reasons discussed in the previous Office Action and herein, the skilled artisan would recognize that some advantage or expected beneficial result would have been produced by the modification of the teachings of Kim *et al.* according to the teachings of Wang *et al.* Thus, the skilled artisan would have been motivated to combine the teachings.

In the second full paragraph on page 13, Applicant contends that there is no evidence of record to suggest that antibiotic selection of transfected cells was considered “time consuming and expensive” as asserted by the Examiner. Applicant asserts that there is nothing to indicate that persons of ordinary skill in the art were seeking to eliminate the use of antibiotic selection.

This argument is not persuasive. As pointed out in the previous Office Action, Kim *et al.* teaches that the obtaining populations of mammalian cells using the antibiotic resistance gene retrofitted BAC clones comprised 3 weeks antibiotic selection. Given that time is consumed and

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resources (including antibiotics, cell culture medium, labor, *etc.*) are used in the process of selection, it is reasonable to conclude that the process is time consuming and expensive.

Finally, in the paragraph bridging pages 13-14, Applicant contends that substituting the amplicon vector of Wang *et al.* for the antibiotic resistance gene retrofitted BAC vector of Kim *et al.* would not eliminate the need for extended antibiotic selection because the method of making the amplicon vector of Wang *et al.* also requires antibiotic selection.

This argument is not deemed persuasive. The assertion made in the *prima facie* rejection is that skilled artisan would be motivated to make the amplicon vector of Wang *et al.* in place of the antibiotic resistance gene retrofitted BAC vector of Kim *et al.* because, once made, the vector provides the benefits resulting from a high efficiency of infection. Although the process of constructing the amplicon vector requires antibiotic selection, this does not negate the expected benefit relied upon for motivation because, once made, the benefits of high efficiency gene transfer are realized each time the vector is used. This is in contrast to the antibiotic resistance gene retrofitted BAC vector of Kim *et al.*, which requires antibiotic selection each time it is used. Furthermore, the fact that antibiotic selection is used in making the amplicon vector of Wang *et al.* does not negate the overall benefit of making and using an amplicon vector relative to the antibiotic resistance gene retrofitted BAC vector of Kim *et al.* because construction of the retrofitted BAC vector also involves antibiotic selection (see especially Figure 1 and the caption thereto and Table 1).

Applicant's arguments have been fully considered but are not deemed persuasive.

Therefore, the claims stand rejected under 35 USC §103(a) as obvious over the art.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

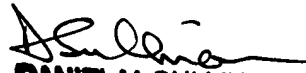
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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Daniel M. Sullivan, Ph.D.
Primary Examiner
Art Unit 1636



DANIEL M. SULLIVAN
PATENT EXAMINER